

**DOCKET NO.:** CP428 (CEPH-3873) (FORMERLY 225326)  
**Application No.:** 10/720,583  
**Office Action Dated:** May 17, 2006

**Amendments to the Specification:**

Please amend the specification by replacement of paragraphs as shown below:

At page 1, please substitute the following paragraph for the paragraph appearing after the heading “**Field of the Invention**”:

The invention relates to an oral pharmaceutical composition comprising modafinil. The composition comprises modafinil particles, wherein at least 5% of said modafinil particles have a diameter greater than 200 $\mu$ . Still, this composition showed dissolution rate and blood levels (after oral administration) comparable with ProvigilPROVIGIL<sup>®</sup> tablets of the same strength.

At page 1, please substitute the following paragraph for the paragraph appearing after the heading “**Background of the Invention**”:

Modafinil, also termed 2-[(diphenylmethyl)sulfinyl]acetamide, is marketed in various countries under brand names such as ProvigilPROVIGIL<sup>®</sup>, ModiodalMODIADAL<sup>®</sup> and VigilVIGIL<sup>®</sup>. It is marketed as tablets containing 100 or 200 milligrams of modafinil. This drug is used for treating conditions of hypersomnia and narcolepsy, namely to improve wakefulness in patients with excessive daytime sleepiness associated with narcolepsy. The drug and its uses were described in the already expired U.S. Pat. No. 4,177,290.

At page 2, please substitute the following paragraphs for the two paragraph appearing after the heading “**Brief Description of the Drawings:**”:

Figure 1 shows the dissolution results of tablets containing 200 mg made in accordance with Example 1 in comparison with ProvigilPROVIGIL<sup>®</sup> tablets of the same strength.

Figure 2 demonstrates the blood level results of tablets containing 200 mg made in accordance with Example 1 in comparison with ProvigilPROVIGIL<sup>®</sup> tablets of the same strength.

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At page 3, please substitute the following paragraph for the paragraph appearing at lines 8 to 17:

Surprisingly, we have found there is a way to expand the modafinil specifications of PSD beyond the limits of '517 US patent and still achieve the desirable dissolution rates of ProvigilPROVIGIL® tablets of the same strength. Moreover, these tablets also showed same blood levels when administered to human volunteers when compared to the blood levels obtained by ProvigilPROVIGIL® tablets of the same strength. This shows that the modafinil tablets obtained by the present invention, having at least 5% of the modafinil particles greater than 200  $\mu$ , are bioequivalent to ProvigilPROVIGIL® tablets of the same strength, not in agreement with the art taught by the '517 US patent. The '517 US patent predicted significantly lower dissolution rates and significantly lower blood levels for such formulations.

Please substitute the following paragraph for the paragraph bridging pages 6 and 7:

The high similarity between the dissolution rate of ProvigilPROVIGIL® tablets and the tablets made by our new invention is an excellent indication for their bioequivalence. The Physician Desk Reference states that "Absorption of PROVIGIL tablets is rapid, with peak plasma concentrations occurring at 2-4 hours. The bioavailability of PROVIGIL tablets is approximately equal to that of an aqueous suspension." Since the absorption of modafinil seems not to be a limiting factor, it is safe to assume that similar dissolution rates indicate similar blood levels (hence similar therapeutic effect) for both products. This was verified by the results of the comparative blood levels in human subjects (see FIG. 2).

At page 8, please substitute the following paragraph for the paragraph appearing after the heading "Example 4":

Dissolution rates of the tablets made according to Example 1, were measured in 0.1N HCl at 37° C and compared to the dissolution rates of ProvigilPROVIGIL® tablets 200 mg. The results are summarized in Table 3.

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At page 9, please substitute the following paragraph for the paragraph appearing after Table 3:

As can be clearly seen, the dissolution rate of the tablets according to Example 1 was similar to the dissolution rate of the ProvigilPROVIGIL® tablets.

At page 9, please substitute the following paragraph for the paragraph appearing after the heading “Example 5”:

The blood vessels of modafinil 200 mg tablet and ProvigilPROVIGIL® 200 mg tablets were compared in regular bioequivalence study. The average blood levels (in µg/ml) of 10 human volunteers are given in table 4.

At page 10, please substitute the following paragraph for the paragraph appearing after Table 4:

It can be clearly seen that the blood level of modafinil at predetermined time periods after administering the tablets according to Example 1 was similar to the blood level after administering the ProvigilPROVIGIL® tablets at the same time periods.